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News & Views

Will the Innovative Medicines Initiative really deliver innovative medicines?

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Put bluntly the sooner academic and industry scientists destroy the stereotypes they hold for each other, the more likely that drug discovery and development will truly evolve to succeed in the 21st century.
Editorial (2006). Nature Reviews Drug Discovery, 5: 267.

A decade ago, seven out of 10 new medicines were developed in Europe but in 2008 this figure has dropped to more like three in 10. Ever-spiralling costs involved in the development of new drugs coupled with highly complex technologies and increasingly specific patient groups have conspired to relegate Europe from its leading position in pharmaceuticals. And that's not forgetting the simple lack of investment in research. Now, the European Commission and the pharmaceutical industry are coming together to overcome some of these barriers and once again push Europe to the forefront of drug discovery.

Launched last year, the Innovative Medicines Initiative Joint Undertaking (IMI) aims to boost investment in European biopharmaceuticals and "overcome bottlenecks" in drug development. Financed equally by the European Commission and the European Federation of Pharmaceutical Industries and Associations, the IMI comes with a budget of €2 billion to cover the period between now and 2013 to be distributed to research projects, the first open calls for which were issued in April.

This year, there are grants of €123 million available for projects in the areas of brain disorders, and metabolic and inflammatory diseases to be allocated through a proposal and peer-review process.

In future rounds of spending, the IMI will move on to target cancer and infectious diseases, areas which have been chosen due to their importance to the health of European citizens and where there is an "unmet need", as deemed by the Commission. A spokesperson for the European Commission said the IMI aims to meet a number of objectives of "critical importance" for EU policy.

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In particular, the IMI's main purpose is to support the so-called Lisbon agenda – a set of goals agreed by EU ministers in 2000 – to make Europe the most competitive and dynamic knowledge society in the world and to meet targets for investing 3% of EU GDP in research and development by 2010. "The pharmaceutical sector in Europe is faced with a number of severe obstacles such as escalating development costs, decreasing productivity, fragmentation of knowledge, difficulties in attracting and retaining a skilled workforce, and lower level of private and public investment than in the other parts of the world, particularly US and Japan," he said.

"In addition, over the past 10 years, Europe's pharmaceutical research and development basis has gradually eroded, with new leading-edge technology research units being increasingly transferred out of Europe, mainly to the United States and recently also to Asia. A key factor for this development is the trend of pharmaceutical industry to relocate to larger markets, where innovation reaps greater awards and where public research spending is highest."

The general idea is that the IMI supports much of the "pre-competitive" research and development processes by encouraging new approaches and technologies to overcome bottlenecks and foster greater collaboration within and between pharmaceutical companies and academia. This pre-competitive research is not so much the development of products themselves but work aimed at improving the tools, information and data that facilitate their development. One example of the type of work that would be a funding candidate are the improvements made in the predictive value of drug metabolism studies in 1990s. In short, the IMI is looking to support useful technologies that companies do not mind being shared among competitors to drive forward the whole industry. "Challenges in biomedical sciences have become so complex that no single research-based pharmaceutical company is able to face them alone. Industries need to join forces with partners to address the main causes of delays in drug discovery," the EC spokesman added.

Currently, US patients gain access to better medicines faster than Europeans with almost 50% of all global new medicines in 2004 launched in the United States.

But, in addition to producing better drugs for patients, the IMI aims to reverse the ''brain drain'' seen in recent years in Europe. Effectively, all those involved in the IMI want to see Europe as a ''big player'' in the international pharmaceutical industry.

According to a 2006 Ernst and Young Global Biotechnology report, in 2005, the US biotechnology industry invested a total of €12.8 billion in research and development, which amounts to 79% of global biotechnology research investment. That figure compares to just €2.7 billion from the European biotechnology industry, a much smaller 16% of global biotechnology research investment.

At the launch for the first calls for IMI research proposals, Arthur Higgins, president of the EFPIA, emphasised the need for collaboration in order for the initiative to achieve its aims. ''The challenges behind innovation are complex, and the decline in the number of new drugs is due to a combination of scientific, regulatory and economic factors,'' he said. ''We as an industry are ready to play our part in bringing forward medical innovation but cannot solve all these issues by ourselves.''

It was the EFPIA who published one of the first documents at the birth of the IMI highlighting the technological problems faced by the industry in getting new drugs on to the market. Estimates put the likelihood of a drug making from the pre-clinical stages through to a product available for patient use at 6% or less.

Not only that, for a single new drug to get through the process it can cost between $400 million and $900 million, experts believe. And, on top of this substantial investment, the process is fairly seriously hampered by the difficulties in predicting safety and efficacy, poor knowledge management and gaps in education and training, the EFPIA warned. Out of these four problem areas grew the Strategic Research Agenda – a document which lays out plans to overcome the barriers and which forms the basis for the IMI's work.

Approved in March after a three-year consultation, it outlines fairly specific recommendations for each. In safety alone, there are a total of nine recommendations ranging from the creation of a European Centre of Drug Safety Research to developing novel methods of risk prediction. It also includes calls to develop biomarkers that will indicate the human relevance and regulatory utility of early laboratory findings; studies of the relevance of rodent non-genotoxic carcinogens; and the development of in silico methods for predicting conventional and recently recognised types of toxicity. For better, faster determination of efficacy and to reduce the current attrition rate of potential drugs, the Agenda lists another nine recommendations (Figures 1 and 2).

In addition to developing in vitro and in vivo models to predict clinical efficacy and in silico simulations of disease pathology, the document urges better integration of translational medicine across industry and academia; regional centres of excellence for validation of imaging biomarkers; co-ordination of national patient networks and databases for clinical trial analysis; and partnership with regulators for developing innovative trial design and promotion of data sharing. Knowledge management is all about defining standards of compatibility across projects, sharing information and identifying those bits of research going on in different areas of Europe but which

Figure 1 – The IMI research agenda is based on four areas to overcome research bottlenecks: *Predicting safety – related to evaluating the safety of a compound during the pre-clinical development; predicting efficacy – addresses bottlenecks in the ability to predict how a drug will interact in humans; knowledge management – the more effective utilisation of information and data for predicting safety and efficacy; and education and training – to close existing training gaps in the drug development process. Source: EFPIA.

are complementary or synergistic to each other. It also includes calls for the development of better tools for exploiting and sharing data. And, finally, to education and training, with plans for a European Medicines Research Academy and an advisory council to develop and promote programmes on medicines development, safety sciences, regulatory affairs and bioinformatics. In total there are 38 recommendations ''to ensure patients benefit from advances in biotechnology''.

So is all this welcomed by those working at the cutting edge of European research? Professor Ulrik Ringborg professor of oncology and director of the Cancer Centre Karolinska, in Stockholm has followed the development of the IMI very closely. ''It's very difficult with increasing complexity of looking at a large number of pathways for potential drugs, for example there are more than 500 different kinases.''

''We're also getting more and more complex clinical trials due to the biological information that's needed. My opinion is that clearer collaboration between the pharmaceutical industry and health care and academia will be very beneficial in speeding up this process. It is no longer the case that clinical trials just compare drug one against drug two or whether patients are responding or not responding, he says.''

''There is a very strong trend to developing pharmaceuticals for which smaller proportions of patients will respond because they are so specific. You need to identify the responding patients and their biological background. For the development of personalised medicine you need patient registers, biological materials, advanced platforms and it's impossible for the pharmaceutical industry – for optimisation you need a collaboration.''

He agrees that Europe, at the moment is too fragmented to deliver the best new drugs and to offer the pharmaceutical industry a good alternative to the US or Asia. ''We have very strong intellectual capital and if we can make translational research more effective and get rid of the barriers we will have an interesting situation. There are some strengths in

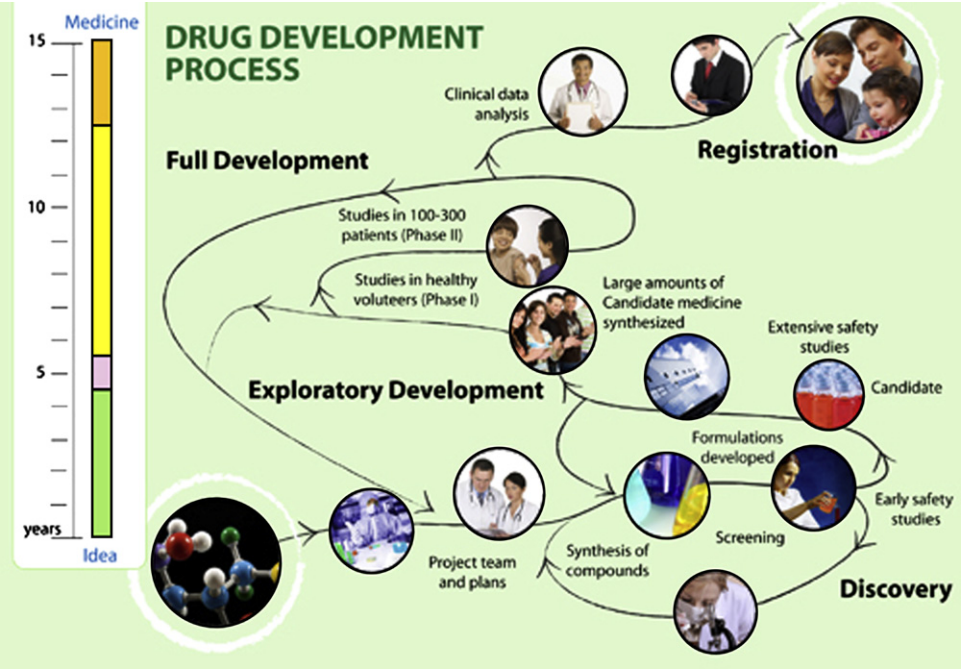

Figure 2 – Schematic representation of the steps involved in the development of a new drug, Source: EFPIA.

Europe which don't exist elsewhere, such as population-based patient registers.''

Professor Ringborg, who is also president of the Organization of European Cancer Institutes believes the IMI does stand a chance of making the proposed changes as long as industry are serious about collaboration. And cancer was quite rightly chosen as one of the areas of ''unmet need'' due to the increasing complexity of research in the field, he adds. ''What is being done in the US with comprehensive cancer centres is a good thing but this is not systematically being done in Europe where you have many small countries and small centres in different cities.''

''We have the problem of critical mass and big American centres have much better critical mass.''

Professor Nadia Harbeck, associate professor in the Department of Obstetrics and Gynaecology, at Technical University of Munich breast cancer said partnership early on in drug development undoubtedly speeds up the process. ''Some companies already team up to develop medicines because the costs are so enormous. We all have to work closer and those of us working in academic institutes, we have to break down barriers of working together with industry – we can't work independently of each other.''

She believes Europe needs a framework such as the IMI to improve equality of drug development and access to drugs at the end of the process. ''In cancer you need biomarkers and there is research necessary at many different levels and some pharmaceuticals' companies are not equipped to do that kind of research.''

She adds that much of what happens in drug development could happen simultaneously if there was a clearer strategy. ''What they have been doing so far is development of drugs and medical tests one stage at a time and that costs an enormous amount to industry and to patients.''

An external evaluation of the IMI published last year concluded if implemented well, it could have a big impact on both industry and society. However, the outcomes of such a large and complex undertaking will not be easy to monitor and some effects may not be seen for a decade or more, the expert group reported.

It stated that if the IMI is to be successful, there must be a swift implementation, sufficient funds, a clear management structure, an IT system worthy of the challenge, collaboration with regulatory bodies, transparency and active marketing of the project.

On the other hand if nothing were done about the problems underpinning the need for the IMI and the biopharmaceutical industry was left to its own devices, the situation would decline with Europe lagging even further behind the US and Asia – particular when other countries are adopting strategies of their own, the report said.

Industry is probably unlikely to invest alone in the pre-competitive phase of research and development and even if they did it would be fragmented.

Speaking after the European Parliament gave support for the Initiative, Janez Potočnik, EU commissioner for science and research called research the ''engine of innovation and growth''. ''By bringing together industry and European public research investment in a specific industrial area under one programme, we boost the chances of making a technological breakthrough putting Europe at the forefront of innovation.''

It remains to be seen whether the next few years will see a turnaround in the fortunes of drug development in Europe but the message seems to be an optimistic one.